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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/258,216	SODERLUND ET AL.	
	Examiner	Art Unit	
	Jehanne S Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *82-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *82,84,85,87,95,97 and 99* is/are allowed.

6)☒ Claim(s) *83,86,88-94,96,98,100 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 82-101 are pending and under examination in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are either newly applied, as necessitated by amendment, or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claim 98 under 35 USC 112/2nd paragraph made at section 5 of the previous office action is withdrawn in view of the amendment.

4. The rejection of claims 82-101 under obviousness type double patenting is withdrawn in view of the filing of a terminal disclaimer.

Maintained Rejections

New Matter

5. Claims 83, 86, 88-94, 96, 98, 100, and 101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER Rejection.

Claims 83, 86, 88-94, 96, 98, 100, and 101 are not supported by the specification for the reasons that follow, and therefore introduce new matter into these claims. Claim 83 is drawn to a method for identifying nucleotide at a predetermined site by hybridizing a detection primer whose 3' terminus hybridizes to a nucleotide 3' ward (on the target) of the predetermined site such that no nucleotide of the same type as the one or more specific nucleotide to be detected be located in the target in any position between the position of the 3' terminus of the primer and the predetermined target position, and extending the primer in the presence of at least one deoxynucleotide and a chain terminating nucleotide such that if a deoxynucleotide is complementary to a specific nucleotide at the predetermined position, a "detectable nucleotide identifier primer extension product" which is detectably different from the detection primer and any alternative primer extension product which would be formed if a nucleotide other than said specific nucleotide were at the target position. Claim 86 drawn to the same method wherein the primer is extended in the presence of at least one deoxynucleotide and a chain terminating nucleotide analogue such that if chain terminating nucleotide analogue is complementary to a specific nucleotide at the predetermined position, a "detectable nucleotide identifier primer extension product" which is detectably different from the detection primer and any alternative primer extension product which would be formed if a nucleotide other than said specific nucleotide were at the target position.

However, a thorough review of the specification reveals that the specification does not describe such methods wherein neither the deoxynucleotide nor the dideoxynucleotide is limited

to be labeled directly, or indirectly as defined at page 17, lines 1-5. Specifically, the specification teaches that the method uses labeled nucleotides that match the variable nucleotide to detect the variable nucleotide in the target nucleic acid (page 7, lines 17-19 and page 10, lines 4-7). Page 10 to page 14, line 5 of the specification describe introducing an affinity moiety into the target nucleic acid during amplification of the target nucleic acid (prior to the detection steps for the variable nucleotide) to allow immobilization of the target nucleic. Page 14, lines 6-28 describe the separation of the amplified target nucleic acid from the amplification mixture. Page 15 through page 16, line 11 describes the detection step primer and teaches that it can be modified to have an affinity moiety different from the affinity moiety used during amplification but teaches that the preferred detection primer is unmodified. Pages 16, line 12, through page 17 line 19 describes the extension of the detection primer. Here the specification teaches that the nucleotide mixture may be one or more nucleoside triphosphate but includes at least one labeled or modified nucleotide which is either a labeled dNTP or a dideoxynucleotide (ddNTP). Page 17 teaches that the dNTP or ddNTP is labeled with a detectable label or modified to have an attachment moiety capable of binding to a detectable label. Page 17, line 20 to page 20 teaches particular embodiments of the invention. Here the specification describes a) a method wherein only labeled ddNTP's corresponding to the variable nucleotide is added; b) a method wherein labeled dNTP corresponding to the variable nucleotide is added and that unlabeled ddNTP is preferably included in this embodiment; c) a method which uses two or more different, differently labeled dNTPs corresponding to the variable nucleotide; d) a method using a detection step primer which is n nucleotides away from the variable nucleotide and using unlabeled dNTPs which are complementary to the n nucleotides between the primer and the

variable nucleotide and labeled dNTPs corresponding to the variable nucleotide which could be substituted for labeled ddNTPs; and e) a method wherein two or more variable nucleotides are identified which requires the use of at least two different detection primers that hybridize 3' of each of the variable nucleotides to be identified. Pages 21-38 describe specific examples and further exemplify labeling with radiolabels, enzyme labels and fluorescent labels.

The specification does not, however, describe a method wherein extension occurs in the presence of at least one deoxynucleotide and one or more chain terminating oligonucleotides wherein neither the deoxynucleotide nor the chain terminator is detectably labeled as is now encompassed by the claims. The specification does not suggest, teach or demonstrate detection in the absence of a detectably labeled deoxynucleotide or one that is "modified so as to comprise an attachment moiety capable of binding a detectable label", but such a method is now encompassed by the claims. The specification is very specific that either the deoxynucleotide or the chain terminating nucleotide analogue is labeled directly or indirectly and the means by which the variable nucleotide is detected. The method described in the specification is directed to detecting nucleotide of known sequence so the base on the deoxynucleotides and the chain terminators for use in the method is predetermined. Consequently, whether or not the deoxynucleotide or the chain terminator will hybridize to the defined site is also predetermined. The specification is clear that either the deoxynucleotide or the chain terminator is labeled (directly or indirectly) in this method. Consequently, the specification does not support the method of claims 83, 86 or claims 88-94, 96, 98, 100, and 101, which are dependent on claims 83 or 86, which encompass that the primer is extended in the presence of a deoxynucleotide or chain terminator which may or may not be labeled.

The response filed 4/1/2004 states that the claims find support at page 7, lines 10-12, which states: "The method of detection of the variable nucleotide(s) is based on primer extension and incorporation of detectable nucleoside triphosphates in the detection step.". The response further asserts that this section does not require that the "detectable nucleoside triphosphates" be labeled. The response additionally asserts that the term "labeled nucleoside triphosphate", not the term "detectable nucleoside triphosphate" is expressly defined, at page 17, lines 1-5. This argument has been thoroughly reviewed but was not found persuasive. Since the specification does not specifically define the term "detectable nucleoside triphosphate", the term is interpreted in the context of the teachings in the rest of the specification. The section of the specification at page 7, which the response points to, when read in context with the paragraph immediately following it, clearly sets forth that the methods of the instant invention require labeled nucleoside triphosphates (which is specifically defined at page 17 to encompass a detectable label or an attachment moiety that binds a detectable label) which match the variable nucleotide and are added such that the incorporation of a label into the detection step primer is measured. The section that the response points to serves to set forth the basis for the instant invention, that is a method 'based' on primer extension and further the incorporation of a 'detectable nucleoside triphosphate'. It is unclear what a detectable nucleoside triphosphate is, other than one which is labeled directly or indirectly, as exemplified by the rest of the teachings of the specification. If the term 'detectable' has some weight or meaning outside the scope of labeled as defined at page 17, lines 1-5, when read in the context of the entire specification, it is unclear how it would differ then from just a "nucleoside triphosphate'. Because the term 'detectable nucleoside triphosphate' is not specifically defined by the specification, when considering this term with the

teachings of the specification as a whole, it is clear that the detection of a primer extension product that incorporates a nucleoside triphosphate other than a "labeled nucleoside triphosphate" as defined on page 17, lines 1-5, is never suggested, described or demonstrated. Instead, the entire specification sets forth methods which detect based on the presence of a labeled nucleoside triphosphate that is 'any nucleoside triphosphate, deoxy or dideoxy, labeled with a detectable label or modified so as to comprise an attachment moiety capable of binding a detectable label" (see page 17, line 1-5). The specification is completely silent as to any specific methods of incorporating a nucleotide triphosphate or detecting a detection step primer that incorporates a nucleotide triphosphate, that is not labeled (wherein 'labeled' is as defined at page 17, lines 1-5) as is now encompassed by the instantly pending claims. Therefore, upon a thorough review of the specification, it is determined that the specification does not provide support for a nucleoside triphosphate that is not either "labeled with a detectable moiety or modified so as to comprise an attachment moiety capable of binding a detectable label".

Response to Arguments

6. The response filed 10/25/2004 traverses the rejection. The response asserts that ample support is found at page 7, lines 10-12 of the specification which states that "The method of detection of the variable nucleotide(s) is based on primer extension and incorporation of detectable nucleoside triphosphates in the detection step...". The response further asserts that this section does not require that the "detectable nucleoside triphosphates" be labeled with a detectable label or be modified to include an attachment moiety capable of binding a detectable label. The response additionally asserts that at page 17, lines 1-5, the term "labeled nucleoside

triphosphate", not the term "detectable nucleoside triphosphate" used in the description of the invention [at page 7, lines 10-12 of specification], is expressly defined to refer to a nucleoside triphosphate labeled with a detectable label or modified to comprise an attachment moiety capable of binding a detectable label. The response concludes therefore, that a person skilled in the art as of the effective filing date of the subject application with the specification of the application at hand would have concluded that the expression "detectable nucleoside triphosphate" as used in the subject application was not limited to the particular definition set out in the specification for the expression "labeled nucleoside triphosphate" since the defined expression 'labeled nucleoside triphosphate" could have been used in the passage at page 7, but instead the expression 'detectable nucleoside triphosphate' was used instead. These arguments have been thoroughly reviewed but were not found persuasive. Since the specification does not specifically define the term "detectable nucleoside triphosphate", one of skill would have interpreted it in the context of the teachings in the rest of the specification. The section of the specification at page 7, which the response points to, when read in context with the paragraph immediately following it, clearly sets forth that the methods of the instant invention require labeled nucleoside triphosphates (which is specifically defined at page 17 to encompass a detectable label or an attachment moiety that binds a detectable label) which match the variable nucleotide and are added such that the incorporation of a label into the detection step primer is measured. The section that the response points to serves to set forth the basis for the instant invention, that is a method 'based' on primer extension and further the incorporation of a 'detectable nucleoside triphosphate'. It is unclear what a detectable nucleoside triphosphate is, other than one which is labeled directly or indirectly, as exemplified by the rest of the teachings

of the specification. If the term 'detectable' has some weight or meaning outside the scope of labeled as defined at page 17, lines 1-5, when read in the context of the entire specification, it is unclear how it would differ then from just a "nucleoside triphosphate'. Because the term 'detectable nucleoside triphosphate' is not specifically defined by the specification, when considering this term with the teachings of the specification as a whole, it is clear that the detection of a primer extension product that incorporates a nucleoside triphosphate other than a "labeled nucleoside triphosphate" as defined on page 17, lines 1-5, is never suggested, described or demonstrated. Instead, the entire specification sets forth methods which detect based on the presence of a labeled nucleoside triphosphate that is 'any nucleoside triphosphate, deoxy or dideoxy, labeled with a detectable label or modified so as to comprise an attachment moiety capable of binding a detectable label" (see page 17, line 1-5). The specification is completely silent as to any specific methods of incorporating a nucleotide triphosphate or detecting a detection step primer that incorporates a nucleotide triphosphate, that is not labeled (wherein 'labeled' is as defined at page 17, lines 1-5) as is now encompassed by the instantly pending claims. Therefore, upon a thorough review of the specification, it is determined that the specification does not provide support for a nucleoside triphosphate that is not either "labeled with a detectable moiety or modified so as to comprise an attachment moiety capable of binding a detectable label". The response uses a section of the specification that does not specify 'labeled nucleoside triphosphate', and recites instead 'detectable nucleoside triphosphate' as support for the lack of any recitation in the claims of a 'labeled nucleoside triphosphate' as defined at page 17 [as well as, it should be noted, for the lack of recitation of 'detectable nucleoside triphosphate']. In effect, the response points to the recitation of 'detectable

nucleoside triphosphate' in the specification as support for a claim that does not even recite 'detectable nucleoside triphosphate', and then concludes that since the specification uses two different expressions, it provides support for a claim that is even broader and recites neither expression. However, when the specification is read as a whole, and the expressions are read in light of the teachings of the specification as a whole, it is clear that the specification is completely silent as to any specific methods of incorporating a nucleotide triphosphate or detecting a detection step primer that incorporates a nucleotide triphosphate, that is not labeled (wherein 'labeled' is as defined at page 17, lines 1-5) as is now encompassed by the instantly pending claims. In fact, the paragraph that immediately follows the paragraph at page 7, lines 10-12, specifically states "Labeled nucleoside triphosphates matching the variable nucleotides are added and the incorporation of a label into the detection step primer is measured" (see page 7, lines 17-19). This paragraph of the specification is referring to the paragraph preceding it (page 7, lines 10-16). No indication is made that the paragraph at lines 17-19 refers to an alternative embodiment. Instead, the specification is completely silent as to any specific methods of incorporating a nucleotide triphosphate or detecting a detection step primer that incorporates a nucleotide triphosphate, that is not labeled wherein 'labeled' is as defined at page 17, lines 1-5. For these reasons and the reasons already made of record in previous office actions, the rejection is maintained.

Conclusion

7. Claims 83, 86, 88-94, 96, 98, 100, and 101 are rejected.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton
Primary Examiner
Art Unit 1634
1/12/05